MICHIGAN
LIBRARY

March, 1952

CLINICAL MEDICINE

for the family physician

Everett C. Fox, Ph.D., M.D.

Works, Inc.
68 Charlton St.,
New York, N.Y.
0652

GOOD REASONS for prescribing . . .

GELUSIL*

'WARNER'

The preferred antacid adsorbent

1. Prompt, effective, prolonged antacid action
2. Nonconstipating
3. Very pleasant taste
4. No complications such as secondary acid rise, chloride depletion, or alkalosis
5. The optimum combination of nonreactive aluminum hydroxide with magnesium trisilicate
6. Available in liquid and tablet form

GELUSIL* Liquid is available in bottles of 6 and 12 fluid ounces. GELUSIL* Tablets are available in boxes of 50 and 100, and bottles of 1000.

WILLIAM R. WARNER *Division of Warner-Hudnut, Inc.*

New York Los Angeles St. Louis

TABLE *of* CONTENTS

59th year of publication

Vol. 59, No. 3 March, 1952

EDITORIAL

The Diagnostic Significance of the Electroencephalogram in General Practice 107
by Frederic R. Stearns, M.D.

ORIGINAL ARTICLES

The Management of Prostatism in General Practice 108
by Russell B. Roth, Anthony F. Kaminsky, and Elmer Hess

Diagnostic and Therapeutic Progress in Allergy 114
by C. J. Sullivan, M.D.

Hyaluronidase in General Practice 119
by J. Schwartzman, M.D.

The Carotid Sinus Syndrome 123
by Elwyn Evans, M.D.

Indications for Surgery of Chronic Peptic Ulcers 127
by Borris A. Kornblith, A.B., M.D., F.A.C.S.

CASE PRESENTATIONS, Thromboangiitis Obliterans . . . 132

DIAGNOSTIC SUGGESTIONS 133

THERAPEUTIC SUGGESTIONS 134

BOOK REVIEWS 136

NEW PHARMACEUTICAL PRODUCTS 137

SEND FOR THIS LITERATURE 138

EVERETT C. FOX, Ph.D., M.D. is Attending Dermatologist, Baylor University and Parkland Hospitals, Dallas, Texas; Consulting Dermatologist, Methodist Hospital and Veterans Administration (Area); Chairman, Council on Medical Economics, Texas State Medical Association; Director, Dallas Health Museum, 1946-1948-1952; Clinical Professor of Dermatology and Syphilology, Southwestern Medical School of the University of Texas; Representative Section Dermatology — AMA House of Delegates, 1949-1952. Dr. Fox is a member of the editorial staff of *Clinical Medicine*. Dr. Fox has written *The Treatment of Acne*, which will be published in the April issue of this journal.

NOW AVAILABLE

CACODYNE

An Isotonic Colloidal
Iodine Cacodylate

Indicated: In all ARTERIAL DISEASES — Coronary, Cerebral, Mesenteric — Hypertension, Angiitis Obliterans.

Frequency of administration is reduced with improvement and gradually withdrawn when symptom free.

For intramuscular or intravenous injection.

No known contraindications.

CACODYNE CREATES
CARDIAC RESERVE

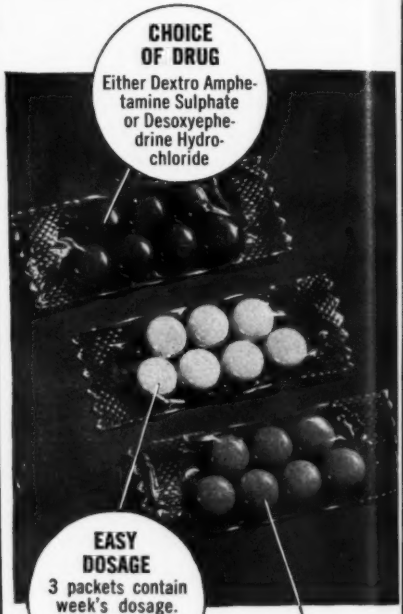
For Reprints and Information Address

RESEARCH MEDICATIONS
INC.

542 Fifth Avenue
New York 19, N. Y.

does your regimen
for management of obesity
offer the advantages of

1·2·3, tablets?


CHOICE OF DRUG
Either Dextro Amphetamine Sulphate or Desoxyephedrine Hydrochloride
EASY DOSAGE
3 packets contain week's dosage. Convenient to carry, easy to take.
EASILY REMEMBERED
color sequence aids patient cooperation. Red, white and blue 3-a-day dosage.

FLEXIBILITY...
Standard formulas offer 1, 2 or 3 gr. thyroid—or none at all—with no change in color sequence. Check these advantages in your own practice without obligation.

Write today for literature and four week clinical trial sample of

1·2·3, tablets

FIRKS
PHARMACEUTICALS
5509 SO. WESTERN AVE., LOS ANGELES 62, CALIF.

EDITORIAL

The Diagnostic Significance of the Electroencephalogram in General Practice

FREDERIC R. STEARNS, M.D., *Editor*

Electroencephalography was discovered as a means of diagnosis by Hans Berger. The EEG records the electrical action currents in the brain; the recording takes place in using electrodes which are placed on the skull or sites close to the head such as the mastoid process or the ear lobes. The electrodes are held in place by a paste which is composed of calcium chloride and bentonite. The entire recording takes about twenty minutes. Generally the standard recording during which the patient relaxes on a couch, is concluded by a period of three minutes of hyperventilation.

An EEG may show the following types of potentials: 1. Alpha waves which exhibit sinusoidal shape and which have a frequency of 8 to 13 per second. 2. Beta waves with a frequency of 15 to 30 per second. 3. Delta waves with a frequency of 6 or less per second; some electroencephalographers do not recognize delta waves. 4. Spikes which are bouts of rapid waves with a frequency of about 50 per second. 5. The spike and wave pattern consisting of alternation of a spike and delta wave.

It is generally recognized that alpha and beta waves are constituents of a normal EEG; some delta waves may appear also in a normal pattern. The appearance of all other waves is pathognomonic for brain pathology.

When there is a difference in alpha acitivity between both sides of the head, it may be due to loss of function of brain tissue on one side such as destruction of a cerebral lobe (traumatic, after operation, after cerebral thrombosis) or in widespread brain diseases such as multiple sclerosis. It should be, however, remembered that deep seated brain processes or small brain lesions may not give an abnormal EEG.

According to some authors, delta activity is prompted by faulty metabolism in the brain cortex, as, for instance, in toxic disturbances, in inflammations or in the ganglion cells close to a brain tumor; it also may appear when the whole cortex is involved, as in encephalitis or in anoxemia of the brain.

The EEG is one of the most important diagnostic means in convulsive disorders. In short, one can say that a grand mal seizure shows fast acitivity of high voltage; the petit mal seizure shows always a typical spike and wave pattern which mostly appears with a frequently of close to 3 per second; the psychomotor seizures on the other hand, display slow activity of high voltage with a frequency similar to that of petit mal seizures. In epilepsy of the Jackson type, the abnormal wave pattern is focalized while it is diffuse in non-Jacksonian epilepsy. It is important to know that epileptics between seizures show abnormal records in up to 90% of the cases. This is particularly true for epileptics of the petit mal and psychomotor type, while epileptics of the grand mal type show relatively frequently normal EEGs between attacks.

The interpretation of an EEG in organic brain diseases is frequently very difficult. Normal records are obtained in organic brain diseases not too rarely, particularly in patients with vascular diseases of the brain, with paralysis agitans, with multiple sclerosis, and even in brain tumors, particularly those of the cerebello-pontine angle and in meningiomas situated above the tentorium. But even gliomos or cancer metastases in the cerebral hemisphere may not show in the EEG. However, in many cases of organic brain disease delta activity is found; yet, because delta activity is encountered in many different conditions, a certain diagnosis cannot be based on this wave pattern.

The electrocardiogram is especially useful in order to differentiate, after a trauma to the head, whether a true cerebral damage or a psychogenic condition persists. While a normal electrocardiogram, however, does not exclude the existence of a previous or a residual damage to the brain, an abnormal EEG will be evidence of such a damage. This is valid particularly for patients with chronic subdural hematoma.

In reviewing the diagnostic possibilities of the EEG, one can say that it is a necesasry means of diagnosis in all doubtful cases of epilpesy of whatever type, and of doubtful trauma to the brain. It is of less value in diffuse organic brain disease while it is an auxiliary diagnostic tool in patients in whom brain tumor is suspected.

BIBLIOGRAPHY

H. Berger. Ueber das Elektrenkephalogramm des Menschen. I. Mitteilung. Arch. f. Psychiat. 87:525,1929.

H. Strauss. J. of Insurance Med. 1:26, December-January-February 1948-1949

W. A. Cobb et al., Electroencephalography: A Symposium on its Various Aspects. Macdonald & Co., Ltd. London, England, 1950

R. Crohn. Clinical Electroencephalography. McGraw-Hill, New York, 1949

F. A. Gibbs and E. L. Gibbs. Atlas of EEG. Vol. I. Addison-Wesley Press, Inc. Cambridge 1950

R. S. Schwab. Electroencephalography in Clinical Practice. W. B. Saunders Co., Philadelphia, 1950

G. W. Smith et al., J. Neurosurg., 7:267, May 1950

H. H. Jasper., J. Pediat. 3:783,1949

ORIGINAL ARTICLES

The Management of Prostatism in General Practice

RUSSELL B. ROTH, M.D.,
ANTHONY F. KAMINSKY, M.D.,
ELMER HESS, M.D.

Erie, Pennsylvania

It is inevitable that with the expanding life expectancy of our population increasing attention must be devoted by the medical profession to those afflictions inherent in the aging process. As more and more life spans extend into the age of prostatism, for example, it becomes more and more pertinent for the general practitioners of medicine to appreciate fully the proper management of the disease.

We have long been engaged, in America, in spirited and sometimes acrimonious controversy as to the proper management of benign prostatic enlargements by the urological surgeon. We have focused perhaps too great a share of our attention on the problems of early operation versus delayed operation and of open operation versus endoscopic resection. It would appear that there might be much to gain in a broader

consideration of the non-surgical aspects of prostatism. Certainly there are questions to be asked. Can anything be done as prophylaxis against nodular enlargement of the prostate? Are all enlarged prostates candidates for surgery? Are there sins of omission or commission in the way cases of prostatism are handled before being referred to the specialist for surgery? And so long as there are questions to be asked there must be virtue in attempting to achieve the answers.

Prophylaxis: Unfortunately it is still possible to dismiss the subject of prophylaxis against prostatism quite summarily. Nothing, to date, in the realm of medication, diet, or general way of life would seem to offer protection against the likelihood of prostatic enlargement. The promising avenues of hormonal approach have led only to disappointment. The use of estrogens, with certain reservations, has been fruitless, The use of androgens has been worse than fruitless—it has been dangerous and destructive. Short of prepubertal castration—a measure certain to want in popularity — there seems to be no practical applicable measure for staving off the development of prostatic enlargement for a significant proportion of the male population which passes beyond the bounds of middle age.

The Enlarged Non-Obstructive Prostate

In the course of a routine general physical examination it is quite common for the physician to encounter a palpably enlarged prostate gland, although the patient has offered no subjective complaints concerning micturition. Any urologist can testify to the fact that the absence of spontaneous complaints is not a reliable basis on which to dismiss a diagnosis of serious prostatism. We have virtually all encountered advanced instances of urinary retention with distended bladders, hydronephrosis, and uremia in individuals who stoutly and even indignantly deny any disturbance in regular urination. It follows, therefore, that when one encounters an enlarged prostate on rectal examination there are certain other things which must be done before this finding may be dismissed. Item one is the determination of the presence or absence of residual urine. In slender, aesthenic individuals simple palpation of the lower abdomen after voiding will often be satisfactory for the demonstration of a substantially empty bladder. In the obese person this is rarely reliable. It would, of course, be possible to check for residual urine by catheterization, but it is one of the theses of this presentation—to be developed later — that catheterization had best be avoided as a casual procedure. It is also quite possible to obtain a graphic picture of the amount of residual urine present if excretory urograms are made if, after the last regular film in the series is made, the patient is instructed to void as completely as possible. An erect film of the bladder area will then show in convincing fashion how much urine remains in the bladder. But excretory urography is scarcely to be considered as a standard office procedure — it is expensive, and, under the circumstances it is unnecessary. A simple intravenous injection of 1 cc. phenolsulphonephthalein can give a rough indication of the presence or absence of residual urine, and at the same time can afford information as to total renal function. Ormond has even devised a useful little formula for application to this test. The patient first voids as completely as possible. Exactly 1 cc. of phenolsulphonephthalein solution is then injected intravenously, and one hour later the patient voids again, emptying out as well as he can. If P represents the percentage of phenolsulphonephthalein excreted, and U represents the volume of urine voided

in ccs, then Ormond's formula $\frac{60-P}{P} \times U$ expresses the approximate volume of residual urine. It may be accepted as a rule of thumb that in excess of 100 cc. residual urine requires attention. Many urologists would place this figure as low as 60 cc. It should be obvious that any major decrease in the one-hour output of PSP would indicate the necessity for more detailed and accurate investigation of impaired renal function.

We may summarize then by concluding that the individual who is found to have a palpably enlarged prostate, but who denies symptoms of prostatism, may be safely dismissed as a candidate for the attentions of a specialist if by palpation or a simple PSP excretion test it can be demonstrated that no significant amount of residual urine exists. Should there still be doubt, the more complicated and more expensive tests may be employed.

It should be added, of course, that in any routine examination the urine should be studied microscopically for the presence of leukocytes and erythrocytes. When pus cells or blood cells are present further evaluation is mandatory.

When the above routine is followed it will be found that many individuals with distinctly enlarged prostates will not be considered as urological problems. This underlines the cardinal fact that it is not the degree of enlargement of the prostate which is the significant factor. It is the location of the enlargement that counts. Small strategically placed enlargements of the median lobe of the prostate may cause extensive obstructive changes, and relatively huge lateral lobe enlargements may be compatible with good health and normal micturition.

The Obstructive Prostate

In general the obstructive prostate is a problem for the urological surgeon. When, by virtue of history, physical examination, and such tests as the physician may choose to make, he has satisfied himself that he is dealing with a truly obstructive gland, he is generally quite content to pass the patient along for the ministrations of the specialist. In a small group of patients this may not be entirely necessary. Prostatic obstruction may at times be caused by congestive swelling rather than by nodular hyperplasia. If this is true the patient may be returned to a normal state by measures designed to overcome the congestion, and surgery may be avoided.

The suggestion that this may be the case is usually to be found in the history. When there is a presumptive connection between the appearance of the obstructive symptoms and episodes of sexual stimulation, alcoholic over-indulgence, or enforced suppression of the normal desire to void one may entertain the thought of a congestive basis. These stories contrast themselves to the gradual and progressive history of increasing obstruction which is due to nodular hyperplasia. When such a state of affairs is suggested by the history, and when one finds on rectal examination an enlarged, rounded, spongy or boggy gland, one may be justified in a therapeutic trial with decongestive measures. These are relatively simple, since they consist of gentle massage of the gland, the application of heat by diathermy or otherwise, and the administration of estrogens—coupled with instructions for the avoidance of the suspected precipitating factors. Perhaps the most controversial measure is the use of estrogens, but it has been an empirical observation with us as with many other authors, especially in the European literature that it is often of some virtue. It is possible that its action lies principally in overcoming the factor of turgidity from sexual arousals.

We come then to consideration of what the physician should or should not do in the matter of care of the patient who is a candidate for possible prostatectomy. The item of principal concern is whether or not the patient should be catheterized prior to hospitalization. It is our strong conviction that catheterization should be avoided whenever it is reasonably possible. We are far happier to encounter a patient with clear uninfected urine as a candidate for surgery than a patient with an already established infection. Since we are considering the patient with an obstructive prostate we are dealing with a situation heavily favoring the development of infection. And it must be admitted that catheterization, even when carried out with the most painstaking technique, provides a mechanism for the introduction of infecting organisms. It must be further recognized that catheterization which is the least bit traumatic may cause edema and swelling which will plunge the patient into acute urinary retention, and which will thereby make an emergency hospital case out of one which might otherwise have been managed more according to the dictates of convenience. We can therefore say that when dealing with the patient who is not in acute retention, who has clear uninfected urine, but who has evidence of vesical neck obstruction, the physician will be wise to avoid urethral instrumentation of any type.

When one is dealing with the patient whose urine is already infected, as demonstrated by gross or microscopic pyuria, it may be quite permissible to use any instrument which is deemed necessary, to determine the presence or absence of strictures of the urethra, to measure residual urine, or for any other purpose that may suggest itself. It only remains to repeat the admonition that the patient with obstructive symptoms and infected urine is almost always a candidate for careful urological investigation.

The Patient in Acute Retention

Any urologist knows of individuals who have experienced an episode of acute urinary retention, who have been catheterized once or twice, and who thereafter experience no further difficulty. It therefore follows that not every case of acute retention is inevitably a case for surgery or specialized urological care. There are, of course, a number of causes other than prostatism for acute urinary retention, and it requires the diagnostic acumen of the doctor to make the differential diagnosis, but in all instances the situation requires immediate action. Acute retention is a most agonizing experience for the patient in contrast to chronic retention which may be virtually void of discomfort. The acutely retentive patient wants relief, and he wants it fast. It might be true that he could be given narcotics for his pain, be tided over the period of acute distress, and carried into the phase of overflow incontinence of urine which can be relatively painless. Though this is possible it is quite obviously undesirable, carrying as it does a severe threat to the anatomical integrity of the bladder, ureters and kidneys, as well as the likelihood of a rapidly developing uremia. Instead the problem is how best the bladder may be drained. For all practical purposes we may discard consideration of suprapubic needle puncture as being a procedure of value, but not one generally adaptable to the requirements of the general practitioner. For him it is usually still best to rely on the catheter.

Catheterization of the acutely obstructed male is not always easy if we may judge the number of hurry calls received by urologists from men in general practice, from hospital interns, and from others who may find themselves in a state of

frustration at their inability to introduce a catheter. We can suggest several things which are worth bearing in mind.

First—Use a local anaesthetic agent. The five minutes invested in instilling deep into the urethra an anaesthetic solution or lubricating jelly is well worth while. It is probably the best single method of avoiding difficulties, since the patient does not resist, does not grab at the doctor's hands, does not tense all his muscles, and, in general, allows the procedure to be carried out with the all-important gentleness which it deserves.

Second — Use a catheter of adequate size, rigidity and shape. He who attempts to stuff a limp slender rubber tube through the obstructed and ofttimes devious urethra is courting trouble. Most urological instruments devised for passage through the urethra are constructed with some modification of the familiar curve of the metal sound. Cystoscopes have elbowed beaks. Metal catheter guides or stylets have assorted curves to aid in passage. And catheter manufacturers provide a multiplicity of sizes and styles. It is well for the psysician who is called on to perform catheterization only occasionally to equip his office and his emergency bag with a catheter which is designed to simplify the job. The woven catheter with a built-in elbow or "Coude" curve is admirable for the purpose. The use of a rigid guide in an ordinary catheter can only be recommended to the individual who fully appreciates that this is one of the most dangerous instruments in the urological armamentarium. It cannot be used in the average whistle-tipped red rubber catheter, and even when used in catheters designed to hold it there is an ever-present possibility of having the stylet tip slip through the catheter eye and penetrate the urethral mucosa. Guides are for experienced instrumenteurs.

Third — Consider leaving the catheter in place for about 12 hours. Each successive catheterization provides additional chance for infection and each one contributes additional trauma. In addition to this the overdistended bladder may be partially paralyzed by the simple fact of overdistension. It may require a short period of rest for the detrusor fibers to regain their normal tonus. A 12 hours rest may be most helpful in accomplishing this end.

Fourth—When removing a catheter, instill an ounce or so of a mild antiseptic solution, of which there are multitudes available. This aids in counteracting any possibility of having infected the bladder, and if a mildly astringent solution such as 1 per cent mercurochrome is used it may have virtue in stimulating the next urination.

If these suggestions and precautions are followed it will be found that a maximum number of cases of acute urinary retention may be restored to normal voiding, and that subsequent studies may be undertaken on an elective basis to determine the necessity for urological treatment or operation.

Symptomatic Treatment in Prostatism

The chief symptom caused by the enlarged prostate is frequency of urination. This is not, in general, a phenomenon caused by irritation but is due to the inability of the bladder muscle to force all of its contained urine out through an obstructed bladder neck at one voiding. This situation will not be influenced by giving chemotherapeutic or antibiotic agents. When infection is not present they should not be used. When infection is present they will only be effective when obstruction is concomitantly eliminated. In short they have little place in the man-

agement of prostatism in general practice.

What is more important to consider is the place of antispasmodics. There is a strong temptation to try to overcome an annoying frequency of urination by giving an antispasmodic medication. Most of these either contain belladonna alkaloids or synthetic substances designed to decrease parasympathetic action. Some, such as Banthine, are potent indeed. A really effective dose of such medication will add parasympathetic paralysis to the already overtaxed detrusor muscle and the patient will be plunged into total retention. If it is appreciated that the frequency of urination in prostatism is due to inadequate bladder emptying rather than to irritative or spastic phenomena it will be readily understood that antispasmodic agents are contraindicated in symptomatic therapy. It may be parenthetically added that more than one ulcer patient who has been getting along quite well with a gradually increasing bladder neck obstruction has been toppled over into acute urinary distress by the Banthine used to treat his ulcer.

Androgens — Testosterone in any and all forms is contraindicated in men of middle age and beyond. It may well be true that in specific instances the indications *for* will overweigh the indications *against* its use, but it may be accepted as fact that one out of every five men in the age of prostatism has cancer of the prostate, and androgens stimulate the growth rate of prostatic cancer. If it were within the power of the physician to examine his patient and assure the fact that prostatic cancer is not present it would be harmless at the worst to try androgens. But such assurance cannot be obtained with any present diagnostic means. Since the use of androgenic substances will not reduce prostatic enlargement it is not only useless but actually harmful to employ them in instances of prostatism.

Indications for Surgery

It will quite frequently fall to the physician in general practice to make the decision as to when a patient needs surgical intervention for his prostatism. There are certain objective findings that make a removal of obstruction virtually mandatory. These are evidences of progressive impairment of renal function, increasing residual urine, and the development of infection. When none of these factors is present it may be reasonable to withhold surgical treatment. One other factor, however, deserves consideration. When nocturnal frequency of urination progresses to the point wherein the patient cannot obtain a full night of rest it stands to reason that accessory symptoms of fatigue, irritability, weight loss, and other even more vague distresses will appear. The restoration of a chance to get a full night of rest will often provide the sought-for solution. Even in the absence of other manifestations of obstructive damage the family physician may be wise under such circumstances to advise urological consultation.

Finally in discussing the role of the general practitioner in the management of prostatism we cannot refrain from commenting that the general physician will do well to avoid predicting to the patient what method of treatment the urologist will consider the best to employ in the given case. The present day urologist usually attempts to suit the surgical approach to the requirements of the case, and such decisions can only be based on observations and data elicited by urological studies.

It is to be noted that we have confined our discussion to the management of *benign* prostatic obstruction. Carcinoma of the prostate is quite another disease from every point of view. Any outline of its management

had best be kept apart from consideration of benign prostatism because of the vast differences in prognosis and course. It would, however, be incomplete indeed to leave any discussion of diseases of the prostate gland without emphasizing the obligation of all physicians to maintain a high index of suspicion of cancer of the prostate, and to remember well that early cancer is curable by radical surgical interference. The hard lump, the nodular gland, in fact any atypical finding is indication aplenty for consultation and a resolution of doubts.

Diagnostic and Therapeutic Progress in Allergy

C. J. SULLIVAN, M.D.

Assistant Professor of Clinical Internal Medicine, St. Louis University School of Medicine

It has often been said that a test for the presence of the allergic state would be highly desirable. The implication expressed in this wish is that, having proven objectively that allergy is present, and moreover having been able to show that it is a factor in the patient's present disability, one could tell whether or not an "allergic investigation" were indicated.

A statement such as this immediately introduces a variety of topics for discussion, such as a strict definition of the allergic state, the subdivisions or various types of allergy, the operation of the allergic mechanism as a feature of non-allergic diseases, the value of a search for an etiologic factor in diseases presently classified as of unknown etiology, and what comprises allergic investigation.

Although a detailed consideration of these topics would provide an excellent exercise, and would also strengthen the foundation of our knowledge concerning the field of allergy, it is doubtful that any irrefutable conclusions could be drawn, since not only the clinical but also the experimental approach to these problems is fraught with difficulties which stem principally from the investigators inability to control extraneous and incidental factors.

Must we then, having raised these topics for consideration, ignore them and side-step the issues? Or is it possible to consider them in the light of present day common sense knowledge? I believe the latter question can be answered in the affirmative, and that all the topics listed above may be fit into this question: "Is there a cause for this patient's disease, and if there is, how can I satisfactorily discover it?" The question may be expressed in the form of declarations. "There is a cause for some patients' diseases, and I will attempt to discover it"; or: "There is a cause for all patients' diseases, and I will attempt to discover it." If a physician accustoms himself to use the latter declaration, it is no longer important whether or not a patient's particular disease is classified as allergic or not; what form of allergy, if any, this disease represents; whether the text book discussion of a particular disease lists an etiological agent or not.

The only important topic remaining is the discussion of what comprises an allergic (or etiologic) investigation, or how can I satisfactorily discover it (the etiologic factor)?

There is a growing tendency in medicine today to treat a disease solely in accordance with the established functional or organic diagnosis. The practitioner too often determines the name of the existent disease and then applies a particular form of treatment. It is the exception rather than the rule for an earnest and conscientious search to be made on the part of the clinician for the etiologic factor of this patient's disease.

In order to discover a given etiologic factor we have certain tools available. These comprise the medical history, the physical examination the thoughtful scrutiny of the progress of the patient, and, least important, the use of laboratory procedures. Diseases due to the direct action of pathogenic micro-organisms are not of course included in this concept of the laboratory's role.

We so often hear about the great importance of the history in the study of a patient that we become accustomed to the dictum and no longer hear it. However, more than fifty per cent of etiologic problems can be solved by a competent history alone, and a large percentage of the remainder can, after their solution by other means, be verified in retrospect by additional history.

In taking the etiologic history it is important to remember that a cause may act several days before its effect is produced. Fortunately, the time interval is usually only about twenty-four hours, and it may at times be measured in minutes. However, when an effect follows in a few minutes the action of its cause, the relationship is obvious to the patient and medical aid is not required for the problem's solution. The greater the "incubation period", the greater is the difficulty in relating cause to effect and solving the problem.

Close questioning in exhaustive detail concerning the patient's activities for at least two days prior to the initial symptom is the proper manner of eliciting the etiologic history. We are concerned only with the moment of the first symptom. Once the reaction has been initiated, the disease process may progress for long periods of time without subsequent contact with the cause, and it is fruitless, usually, to concern ourselves at this point of the history, with progress of the disease.

The patient's activities under scrutiny not only pertain to diet and drugs but, most important of all, to his environmental changes. A short nap on a day bed, or a visit to the basement or the attic, may, and often does, provide the opportunity for the cause to act.

Causes which are environmental in nature are often seasonal. This is most often observed in seasonal asthma, occurring in late Spring and again in September or October. These patients almost always lose their asthma when hospitalized. Pollen alone cannot be the causative factor, for hospitals are not pollen-free. But hospitals provide an environment far different from that of the modern home. Moreover, these patients are able to tolerate their environment without trouble during the other seasons of the year.

Not all environmental causes act seasonally, however, and in these cases it is more apparent that the present residence is related to the cause of the patient's trouble.

The physical examination may disclose the existence of distant disease The inter-relationship of diseases operates in an obscure manner. For example, we cannot at present conceive of the mechanism whereby chronic cholecystitis may be causatively related to chronic urticaria. Nevertheless, we are justified in considering the patient as a whole, and supposing that the existence of one disease process may upset the entire mechanism of defense, allowing for the development of distant, more readily recognizable disease. Focal

infection is a poor term as a concept of this mechanism; generalized defense disturbance is better, but not much better.

The patient's progress can often tell the whole story. Within certain limitations it is possible for the physician to effect withdrawal and controlled re-exposure to almost any potentially etiologic factor. This is applicable to any food, any drug, and most environmental factors. However, unless the physician is aware of the natural course of the disease under study, he may gain more misinformation than information from this procedure.

An example of the confusion that may arise is this. We shall use as illustration a patient with asthma due to aspirin, and assume that the cause is unknown to both patient and physician. This episode of asthma may persist two weeks and then, having run its course, subside. During the first week the physician may withdraw all drugs (including aspirin); the disease continues and aspirin may falsely be exonerated as the cause. Near the end of the second week, eggs may be withdrawn from the diet. Within a day or two the disease terminates and egg is erroneously attributed to be the cause.

How can this confusion be avoided? The best method is to require certain proof. In the above case, purposely feeding eggs during an asymptomatic period would show that this food was inoccous to the patient. A knowledge of the natural history, i.e., of the possible protected length of an asthmatic episode, should require that everything eliminated during the two week period as well as everything contacted during the two or more day interval preceding the episode of asthma, is suspected of being the etiologic factor.

The most difficult disorders for the successful employment of this approach are these states of continuous clinical disease. An example of this is perennial bronchial asthma. Since complete termination of the disorder is at times not possible, it is difficult to evaluate purposeful re-exposure. At times, unfortunately, it is necessary to evaluate degree of exacerbation. So-called structural changes, such as emphysema or fibrosis, having occurred, preclude the reversion to complete normal. Moreover vigorous and protracted therapy is often required to effect a base-line of minimum symptomatology. Nevertheless, it is almost always possible to reach this base-line eventually, and having reached it, to attempt to evaluate the effect of re-exposure to factors under suspicion. If this is carried out with a high degree of criticism in evaluation of change, it is often gratifying to detect such a change, and to be able to demonstrate it repeatedly which is, of course, a requisite for final pronouncement of guilt.

The role of the laboratory is not a large one in the type of diseases under discussion. Its chief use is in the establishment of the diagnosis of the disease process. It offers very little assistance in the detection of the offending factor, which is our primary concern here. Skin testing is a laboratory procedure. Since the immediate reactions, the ones in which effect follows very rapidly after exposure to cause, are rarely profound problems in etiologic diagnosis, and since these disorders are the ones where positive skin sensitivity normally exists, there appears to be very little justification for the employment of skin testing in this group. There are exceptions, such as the case of May hay fever. Is it due to a tree or grass pollen, and if a tree, is it oak or some other tree?

But the delayed clinical reactions are frequently unassociated with immediate type of skin sensitivity. It is true that delayed positive skin reaction may often occur, but if so,

there are usually multiple delayed reactions, all of which may be clinically unrelated to this disease in question. Moreover, the skin test may of itself introduce sufficient specific antigen to produce a delayed constitutional or focal reaction. It is often undesirable to complicate the clinical course with a possible induced reaction, although under carefully controlled conditions this might not be undesirable, but actually helpful. However, in such a circumstance, there is full realization of what is being done, which removes the procedure from the appellation of "routine skin testing".

It is to be recalled that the pathology of allergic reactions that are delayed in their occurrence after the impact of the cause, resembles, in some respects, the pathology of some chronic inflammatory disorders, such as tuberculosis. In this latter there is no circulating antibody that gives an immediate positive skin test reaction. False negative skin test reactions in tuberculosis would always occur if an aqueous extract were used for testing and the reaction read in fifteen minutes. As for the employment of delayed readings of ordinary "allergic skin tests", we must remember that the delayed positive tuberculin skin reaction tells us little or nothing about the patient's present disorder, and the same thing would hold true in delayed positive "allergy skin tests".

II Therapeutic Progress

Everyone is familiar with the beneficial effects of Cortisone, ACTH, the antihistaminic drugs, the antibiotics, and intravenous aminophylline in the treatment of allergic diseases. The important question today is this: Can the patient with chronic allergic disease be satisfactorily managed by employing one or more of the above listed therapeutic agents without recourse to etiological management? In answer to this question, let us propose a case of asthma caused by contact with feathers. Cortisone or ACTH might very well suppress the asthma even with continuous contact of the patient with feathers, and both patient and physician might be eminently satisfied with the result. However, were it possible to terminate the asthma simply by removing feathers from the patient's environment, one could hardly agree that Cortisone administration was the best way of treating this patient.

In our discussion of the diagnostic aspect, we have stressed the importance of searching for the cause. If it can be discovered, it should be removed, if that is possible. However, this is not always possible and this presents an intricate problem. The alternative of employing "desensitization" must be considered.

The first problem for discussion here is that of specificity of antigens. If the cause is known to be an environmental factor, what is the importance of detecting the specific factor, in order to employ an extract of it in "desensitization"? Let us propose another case of bronchial asthma. It has been necessary to hospitalize the patient, where he either became asymptomatic or improved greatly. The patient is discharged and shortly after returning home redevelops his trouble, or it is definitely aggravated. His environment has been changed, in so far as possible, in an attempt to remove all but the most austere furnishings. Moreover, his trouble is perennial, so that seasonal air-borne material can be largely exonerated. The exact nature of the cause escapes detection.

In such a case it has been the experience of many investigators that a stock extract composed of a variety of potentially etiologic agents may be employed. These stock extracts are called house dust extracts. They are composed of a mixture of substances, by reason of

their origin including not only particles of cotton, kapok, wool, silk, feathers and various animal hairs, but also fungi and saprophytic bacteria. The soluble substances from all of these materials are present in the final extract.

It is unfortunate that diseases such as chronic bronchial asthma or chronic rhinitis or chronic dermatitis do not, in their response to therapy, lend themselves to statistical evaluation. It has been a clinical observation for years that the natural history of these diseases is one of fluidity and fluctuation. Improvement or even disappearance of all symptoms may occur "spontaneously." Therefore, improvement or cure occurring during a certain form of therapy is not acceptable as conclusive evidence of the efficacy of the particular form of therapy employed.

However, in cases of prolonged duration it is almost always possible to plot the past course of the disease, and from this information one should be able to predict, with at least some degree of accuracy, what the future course would be. In such a case, when the future becomes relatively or absolutely asymptomatic, it is probably permissable to suspect that the therapeutic measures employed were related to the improvement. This type of reasoning is particularly applicable when the same physician has observed the patient over both his past and future course. A change in therapeutic regimen is much more likely then to be correctly held responsible for the patient's improvement.

Controls are not a satisfactory tool in observation of this problem, unfortunately, since it is difficult to find a series of such cases which are exactly alike in their natural clinical course.

At the present time, it is necessary to formulate opinions concerning the efficacy of a therapeutic measure on the reported experience of those physicians who have studied the therapy in detail, together with personal experiences of the physician currently employing the therapeutic tool.

There are reports in the literature of clinical improvement following the use of stock house dust extracts in cases such as the environmental patient cited above. Our next concern is with the method of administration of the extract. The literature on this phase is confusing in the wide variety of schedules of dosage that are recommended. At the present time, one thing appears fairly certain: Overdosage is responsible for innumerable treatment failures. The converse is not necessarily true: that properly small dosage will always produce treatment cures. However, small quantity given at long intervals has been found to be clinically satisfactory in the hands of some investigators.

What then is the proper interval between injections? If a single injection of extract is administered and the patient is observed closely, one is often surprised to observe the development of a new symptom, the recurrence of an old symptom, or an exacerbation of the patient's chief complaint, about two weeks later. Obviously, there is no way to be certain that this is the effect of the injection. However, when one observes this happening in several patients, one is justified in suspecting a relationship between the two.

It would seem wise to wait until this possible reaction had passed before readministering the extract. Therefore, intervals of about once every four weeks seem to be, in at least some individuals, the safest treatment interval. One has only to recall that there have been a few reports of deaths suspected to be related to frequent re-injections, and many reports of severe exacerbation of the chief complaint following too zealous injection administration.

It is true that this two week possible reaction is not universal, and that many patients are able to receive frequent injection without harm, but we are not in a position to foretell this in advance of therapy. therefore, extreme caution should be the watchword.

The size of the dose should be small. Since we begin with a heterogeneous mass in the preparation of the extract, there is no basis for sensible measurement of "active principle". One to one million dilution of a concentrated extract is probably a satisfactory starting point.

Increase in the size of subsequent doses is perhaps desirable. The doctor must weigh and balance his patient's response in attempting to gauge future doses. He should appreciate that what he is doing is obviously not desensitization in its strict immunologic definition, and be little concerned about dosage increment.

Without attempting to enter a discussion about bacterial allergy, it may merely be stated that bacterial extracts and vaccines are widely employed in desensitization, often in patients whose course closely resembles that of the asthmatic described above, in whom it was decided that house dust extract should be employed.

Everything that has been said about dust extract dosage and interval applies also to therapy with bacterial products. The similarity of the two types of extract suggest that perhaps complex polysaccharides derived from the two sources may be antigenically related, or else that micro-organisms contribute largely to the active principle of house dust extracts.

Lastly, it should be pointed out that all the measures listed in this discussion are often necessary in the management of a single patient. Usually, there is no short-cut to the satisfactory control of the chronic allergic individual. However, since the number of favorable clinical responses usually surpasses the number of treatment failures, it becomes obvious that it is desirable to include, along with other therapeutic measures, the plan of searching for the cause, removing it if at all possible, or "desensitization" when removal is not possible.

Hyaluronidase in General Practice

J. SCHWARTZMAN, M.D.

From the Department of Pediatrics of the New York Medical College, Flower-Fifth Avenue Hospitals and Metropolitan Hospital, New York City, N.Y.

Introduction

One of the newer medicaments that has attained great usefulness is hyaluronidase. Although first discovered in 1929, its value was not begun to be appreciated for at least another decade. At present, it has become one of the most promising medicinals and numerous investigations concerning it have been and most likely will continue to be carried out.

Definition and Mechanism of Action

Hyaluronidase is a mucolytic enzyme which depolymerizes the mucopolysaccharide acid, hyaluronic acid. The latter is a gel, found in the ground substance of connective tissue, which binds fluid in the in-

terstitial spaces, prevents its diffusion by keeping cells together in a viscous like matrix and aids in the regulation of the exchange of metabolites. As a result of its activity, fluid absorption in hypodermoclysis has been accelerated from 5 to 14 times[1-4]. However, this reaction is reversible[5] and the hyaluronic acid barrier is partially reformed in 24 hours and almost completely restored in 48 hours.

Sources

Hyaluronidase has been obtained from numerous sources such as bacteria, leech extracts, bee, snake and spider venoms, spermatazoa and mammalian testes.

Standards of Measurement

The content of hyaluronidase can be determined and expressed by any of the following methods:

1. Viscosimetry:—which measures its ability to decrease the viscosity of products containing hyaluronic acid. One unit is the amount necessary to reduce the viscosity to one half within 30 minutes.
2. Turbidimetry: — measures the ability to reduce the turbidity of a solution containing hyaluronic acid. One turbidity unit is that amount which decreases the turbidity caused by 0.2 mg. of hyaluronic acid in horse serum to that caused by 0.1 mg. of hyaluronic acid without hyaluronidase.
3. Mucin clot prevention:—measures its ability to prevent the formation of a fibrous mucin clot which results from the action of a substrate protein upon the addition of acetic acid.
4. Diffusing activity in the skin:—measures its ability to diffuse India Ink such as blue dye T-1824.
5. Weight in micrograms.
6. Therapeutic efficiency: — measures that amount of hyaluronidase in a given product, which, when utilized in hypodermoclysis with a fixed amount of a given solution, gives the most dependable optimum absorption time.

Method of Administration

In hypodermoclysis, the procedure that has been found to be most effective is the following:

Having found the patient nonsensitive to a skin test, ordinary gauge hypodermic needles are inserted into the sites selected. The clysis is started, and 5 to 10 cc of the fluid are permitted to flow through each side. Then 500 viscosity units (which has been found to have the greatest therapeutic efficiency[6] are injected into the lumen of the rubber tubing about one inch from its junction with the needle. This distributes the hyalyronidase in good concentration and over a wide area early in the clysis. Following this, the clysis is permitted to run freely at the rate desired, usually administering 150 to 200 cc per kilogram of body weight per 24 hours. By regulating the height of the level of the infusion fluid to about 12 inches above the infusion area, there will be a slow, steady drip with a steady rate of absorption. In pressure clyses of small amounts of fluids or drugs, the enzyme can be added to the solution being administered. In general with this technique, 250 to 300 cc of electrolyte solution can be given rapidly within 80 minutes.

Indications

1. It is of great value in hypodermoclyses of electrolytes[1], plasma[7], serum[2] and heparin[8].
2. It has been found beneficial in local anesthesia for
   a) Surgery[9] and ophthalmology[10, 11].
   b) Infiltrative anesthesia[9] for ankle sprains, myositis, subdeltoid bursitis and dental surgery.
   c) Increasing the diffusion of the local anesthetic agent in pudental blocks[12] and tonsillectomies[13].

3. It is of value in the prevention of painful arms resulting from the accidental injection of neoarsphenamine, mapharsen[14] or similar substances.
4. It can facilitate the rapid resorption of painful hematoma[8].
5. It may reduce the viscosity of exudes in joints[15], and in pleural and peritoneal cavities[16]
6. It may aid in the flattening of areas of mucinous infiltration of the skin[17]
7. It has been found useful in the intramuscular dye injections for pyelography[18,20] for infants and children.
8. It increases the penetration of penicillin through mucous membranes[21] when combined with it prior to its instillation into the paranasal sinuses.
9. It has been found useful in some cases of infertility[22,26] especially when associated with a decrease in the hyaluronidase content of the semen.

Contraindications

1. It should not be used in any individual who is allergic to the product.
2. It should not be used when the total protein in the body is decreased below 5.3 mg. percentage[6] since the fluids will enter the tissue with increased speed but there will be delayed absorption into the blood stream.
3. It should not be used in septicemias unless chemotherapeutic agents are being used concurrently.
4. It should not be injected directly into area of localized injection.

Failure of Action of Hyaluronidase

In situations where hyaluronidase does not appear to be effective, any of the following factors may be involved:—

1. Marked physiochemical alterations within the body as when the total proteins are below 5.3 mg. percentage.
2. Ineffective or inactive enzyme resulting from deterioration of the product which has remained in solution more than 14 days.
3. Absence of hyaluronic acid in the area concerned and therefore no effect from the enzyme.
4. Presence of hyaluronidase inhibitors in large enough quantity to counteract it.
5. Physical factors such as local heat can delay its influence on absorption.

Sensitivity and Toxicity

Intradermal skin testing[27] with the finest products available to date revealed only 0.08% positive skin tests.

Relative to its toxicity, all observers agree that it is insignificant. There has been no evidence of any thermal reaction or dispersion of pre-existing infection provided it is not injected into the infected area[28]. It has also been shown to have no detectable effect on temperature, pulse, blood pressure, blood count, urine and phenosufonphthalein tests [18, 28, 30]. In addition no abnormalities were observed in the kidney, liver or blood.

Advantages of Its Use

1. No intricate setup is necessary.
2. No experienced personnel is required.
3. It can be utilized in the home, in the field or in the ambulance.
4. It can be started without any delay.
5. The flow can be accommodated to the need.
6. The procedure can be stopped for any length of time without any concern regarding clots obstructing the needle. It can be restarted at any time and if required pressure can be safely applied to the rubber tubing or directly to the needle to restart the flow.

7. There is no danger[31] of thrombosis of veins or emboli since the circulation is not directly involved.
8. There is an absence of pyrogenic or other untoward circulatory effects[31] such as phlebitis, ascending infections, and cardiovascular and pulmonary disturbances.
9. Toxicity and sensitivity are almost negligible.
10. It increases the absorption of fluids by 5 to 14 times more than ordinary clyses.
11. It is much more humane since it decreases the duration and intensity of pain during fluid administration.
12. It is of very great value in cases in which intravenous therapy is impractical, difficult or inadvisable because of the status of the patient's veins as might occur in infants, small or obese children or in hemorrhagic disturbances; or because of failure of cooperation of the patient as in insanity or convulsive states.

Summary

1. Hyaluronidase facilitates fluid absorption by 5 to 14 times.
2. Sensitivity and toxicity are extremely low.
3. It is of greatest value in clyses, subcutaneous administration of drugs, intramuscular pyelography, sterility, and in local anesthesia for surgery, dentistry, ophthalmology, tonsillectomies and pelvic procedures.
4. At times failure of its action may be attributed to either an ineffective enzyme, excessive presence of inhibitors or abnormal physical or chemical conditions of the body as previously enumerated.
5. The precautions advocated should be exercised in its use during sepses, localized infections or associated physiochemical changes in body constituents such as total proteins.
6. Numerous advantages of its use have been cited.

Conclusion

With the advent of hyaluronidase, another wonderful therapeutic agent was placed at the command of the medical profession. It has made fluid administration an easier and more pleasant procedure. It is the best and most efficient substitute for intravenous therapy when the latter is unnecessary, difficult to perform or contraindicated. However, it does not in any way displace nor make obsolete the use of intravenous therapy, for the latter is still a life saving measure when the utmost in speed in fluid administration is vital. However, because after intravenous therapy, it is the next fastest method of fluid administration and because it is so easy to administer and because it is more humane, it should find more frequent use in the earlier stages of fluid disturbances so as to prevent the critical need for intravenous therapy.

(Editorial note: references identified upon request)

SIDE GLANCES at MEDICAL HISTORY

WILMS TUMOR

It appears that the embryonal adenosarcoma of the kidneys was not first described by M. Wilms (1867 to 1918) but by C. J. Eberth in his paper Myoma sarcomatodes renum. Virchows Arch. f. path. Anat., 55:518, 1872.

The Carotid Sinus Syndrome

ELWYN EVANS, M.D.
Orlando, Florida

The carotid sinus is a dilatation of the common carotid artery where it bifurcates into the external and internal carotid arteries. The dilatation also usually involves the internal carotid artery as well and occasionally is confined to this area.

It has been known for many years that pressure in the region of the carotid sinus might produce slowing of the heart, unconsciousness, and convulsions. These effects were ascribed to stimulation of the vagus nerve until the anatomic and physiologic studies of Hering[1, 2] who described the role of the carotid sinus in regulation of the heart rate and blood pressure.

Weiss and Baker in 1933[3] called attention to the fact that a hypersenitive carotid sinus reflex was responsible for some spontaneous attacks of vertigo, syncope, convulsions, and lesser symptoms. Carotid sinus syndrome should be differentiated from the hyperactive carotid sinus reflex; the former is associated with syncope, but the latter is not. Weiss and Baker described 3 types of carotid sinus syndrome: (1) the cardio-inhibitory or vagal type with cardiac slowing or asystole which is prevented by atropine; (2) the vasodepressor type in which there is a decided drop in blood pressure not related to bradycardia which may be prevented by epinephrine but not atropine; (3) the cerebral type in which there is loss of consciousness without significant cardiac slowing or drop in blood pressure and is not affected by atropine or epinephrine. Ferris and his co-workers[4] found 34 per cent to be of the cardio-inhibitory type, 5.3 per cent of the vasodepressor type, and 60.7 per cent of the cerebral type. They also described mixed forms. Procainization of the carotid sinus abolished all types.

Spells of unconsciousness may occur abruptly but a definite aura usually is present; dizziness, weakness, spots before the eyes, ringing in the ears or epigastric distress may precede the attack. Hyperpnea, perspiration, and pallor usually occur and vertigo is prominent[5] during the attack. Attacks usually last from a few seconds to 15 or 20 minutes but average 1 to 4 minutes. The patient usually feels well between attacks; however, 2 cases have been mentioned in which fatigue persisted for a day or more after an attack[3, 6].

Despite numerous publications, the hyperactive carotid sinus is still an important and perplexing problem.

Etiology

There is no satisfactory explanation why the carotid sinus becomes hyperactive in some patients, although we do know that there are several predisposing factors including age, sex, vascular disease, especially cerebral and cardiac, medications fatigue, emotional states and organic diseases which increase vagal hypertonicity. It is also possible that there may be some familial predisposition[7] and that changes in the wall of the sinus itself play a part[6].

All reports emphasized age and sex. Males ranged from 85 per cent[8] to 94 per cent[4]. Draper[9] in reviewing 59 cases reported in detail found 51 or 86.5 per cent to be males. In a series reported by the author[6], 9 out of 10 were males.

Of the 59 cases of carotid sinus syndrome reviewed by Draper[9], 2 were in the third decade, 4 in the

fourth, 6 in the fifth, 20 in the sixth, 21 in the seventh, and 5 in the eighth. In the author's series[6] ages ranged from 43 to 77 years, averaging 57.5 years. Hyperreactors also predominated in the upper age brackets. Seventy per cent of Nathanson's 115 cases were between 50 and 70 years of age. Incidentally, 77 patients or 67 per cent were without symptoms suggestive of carotid sinus syndrome. Sigler[10] testing 1,151 males and 735 females, found that the incidence increased in adult life and reached a fastigium in middle life.

Various drugs are known to accentuate carotid sinus sensitivity, especially the vagal type[4,11,12,13,14]. These include mecholyl, morphine, digitalis, nitrites, caffeine, calcium, niacin, nicotine, strychnine, thyroid extract, eserine, salicylates, potassium cyanide, and light chloroform anesthesia.

Heart disease predisposes to carotid sinus irritability, especially the cardio-inhibitory type. Sigler[10] found that 93 per cent of the patients with demonstrable coronary sclerosis showed significant bradycardia on carotid sinus pressure. Seventy-five per cent of those with significant hypertension, but without demonstrable coronary sclerosis, showed significant bradycardia; 79 and 55 per cent showed definite response respectively in groups with cardiac disease other than arteriosclerotic and groups without heart disease. According to Nathanson[15], 34 of his first 40 patients showing cardiac standstill following carotid sinus pressure had angina, and one-third of the patients with coronary disease and angina were hyperreactors. Sigler[16] stated that a high degree of carotid sinus hyperactivity rarely occurred in the absence of coronary disease and that local ischemia diminished resistance of the ganglions and myoneural junctions in the heart or produced local chemical changes that sensitized the vagus system in the heart.

The carotid sinus reflex varied with the heart rate[17]. The reflex was absent in patients with marked bradycardia, greatest in patients with moderate bradycardia and greatly diminished in those with tachycardia. Increased vagal tone increased the activity of the reflex up to a certain point beyond which it decreased. Vagal tonicity increased with age.

Nathanson[8] attributed the cardio-inhibitory response predominantly to vagal hypersensitivity, although he stated that it was possible that the structure of the carotid sinus in some persons was such that intra-sinal pressure changes were easily transmitted to the sensory endings in the adventitia resulting in cardiac inhibition and symptoms. The author[6] found that the right carotid sinus was more dilated and more sensitive than the left in 5 patients in whom the sensitivity of both sinuses was checked. He also found varying degrees of sclerosis of the sinus in 8 of 10 patients with syncope. It is of interest, however, that many patients with sclerosis of the carotid sinus show no hyperactivity.

According to Sigler[18], individuals who suffered from cerebral arteriosclerosis showed the most alarming cerebral symptoms.

Jones [19] reported a case in which inflammatory regional lymph nodes were a contributing factor.

Engel and Engel[20] found that 18 (78 per cent) of 23 patients with acute symptomatology arising in the biliary tract showed cardiac standstill of 3 seconds or more after carotid sinus massage. Carotid sinus hypersensitivity disappeared in 7 out of 10 examined postoperatively. They interpreted this as showing summation of afferent impulses from end organs in the biliary tract, which had reached the threshold of reaction of vagal centers in the medulla.

Several investigators emphasized emotional upsets, worry, and neurotic

states in the cerebral form [3,4,21]. Bronson and Stuart observed a high incidence of associated disorders including emotional instability. Purke[22] stated that emotional tension was known to increase reflex irritability. Evans[6] emphasized the importance of emotional factors in the cardio-inhibitory or vagal form. He also stated that tension states and vagal hypertonicity were frequently associated in gastro-intestinal disorders so that it was not surprising to see such a close relationship between tension states, vagal hypertonicity and the vagal type of carotid sinus syncope as well as between tension states and the cerebral type. Variation in such states could readily account for some of the variability in the sensitivity of the carotid sinus. It is possible, however, that variation in the cerebral factor played a part in apparent vagal forms because the 2 factors often co-exist[3,4,23]. Galdston, et al[23] found that 2 or more types usually occurred simultaneously, but 1 type predominated. They also mentioned cases in which syncope and convulsions occurred on stimulation of the side which produced the lesser degree of circulatory change and failed to occur on the side which caused more marked circulatory response. Evans[6] reported a case in which the cerebral form predominated on 1 occasion and the vagal on other occasions. That cerebral factors played a part in many patients with vascular response was shown by Lennox et al[24], who demonstrated that even in patients with cardiovascular responses the degree of cerebral circulatory slowing was not as marked as could be produced by other procedures which did not result in loss of consciousness.

Precipitating factors include turning the head, looking up, shaving, tight collars, or anything causing pressure on the carotid sinus area. Smith and Moersch[25] found precipitating factors in only 25 per cent of 35 patients. Draper[8] in reviewing 59 cases found precipitating factors in 30 per cent; the most common factors were sudden movements of the head, assumption of the erect position, coughing or straining at stool.

Incidence

The incidence of spontaneous major seizures is unknown but it certainly is not uncommon, especially in males with coronary disease in the upper age brackets. Cope and associates[26] described 11 cases seen during a period in which they saw 11 patients with peptic ulcers, 4 with diabetes, 3 with active pulmonary tuberculosis, 10 with syphilis and 1 with pernicious anemia. Weiss and Baker[3] reported 15 cases in 1933 and observed a total of 56 in the next 3 years[4]. Smith[27] reported 85 cases at the Mayo Clinic by 1937.

Overactivity of the carotid sinus without syncope is doubtless common. This is also affected by age, sex, vascular disease and other factors. In the general population, 60 to 80 per cent would probably show changes in the pulse rate, blood pressure, or electrocardiogram on pressure over the sinus[24]. Nathanson[8] stated cardiac inhibition was as intense and easily elicited in the asymptomatic group as it was in those with symptoms.

Diagnosis

Diagnosis is made from the history and by inducing an identical attack by pressure on one of the carotid sinuses. While the sensitivity of the carotid sinus is being tested, the patient preferrably should be in the sitting position with the head tipped slightly backward and turned away from the side being examined. The sinus usually is situated below the angle of the jaw at the upper border of the thyroid cartilage. Sometimes the carotid bulb is readily palpable. Pressure is gradually made with the thumb so that the sinus is compressed against the spinal

column[28]. Sudden pressure is undesirable, especially in some elderly patients with considerable arteriosclerosis, and massage should be avoided[8]. Unduly prolonged pressure may be fatal[29]. As a rule characteristic response will occur in 10 to 25 seconds. Bilateral stimulation is dangerous[21] and repeated stimulation should not be done after diagnosis is made because of occasional serious complications[30,33]. Askey[31] described 7 cases of hemiplegia which occurred immediately after carotid sinus pressure.

Carotid sinus syncope should be considered in the differential diagnosis of all cases in which dizziness, faintness, and unconsciousness, with or without convulsion, occur. Other conditions which frequently must be differentiated are idiopathic epilepsy (petit and grand mal), narcolepsy, cataplexy, postural hypotension, hypoglycemia, various cardiac disturbances associated with asystole, tachycardia of various sorts and aortic stenosis, and vasovagal syncope. The latter is the most common cause of syncope and its relation to sudden emotional stimuli such as the sight of blood, fright, pain, etc., is usually clear. In postural hypotension, the drop in blood pressure and transient unconsciousness are associated with assumption of the upright position. Although carotid sinus syncope may be precipitated by pain or assumption of the upright position, it may be differentiated from the previous conditions by being reproducible on carotid sinus pressure. Spontaneous hypoglycemia usually occurs 2 to 4 hours after meals and is associated with a low blood sugar. Weiss and Baker[3] and Freedberg and Sloan[34] were unable to find any relation of the carotid sinus to idiopathic epileptic seizures. Because carotid sinus syncope is frequently associated with cardiovascular disease [8,21,35], differentiation in combined cases is not always easy. Various degrees of heart block are sometimes persistent in patients with Adams-Stokes attacks. Tachycardia, auricular fibrillation or flutter may be noted during attacks in patients whose unconscious spells are associated with these disorders. Occasionally other diseases especially Ménière's Disease may complicate the picture and make the diagnosis more difficult[6,36,37]. Syncope cannot be produced by carotid sinus pressure in uncomplicated cases of heart disease or Ménière's Disease.

Prognosis

Prognosis of patients with a hyperactive carotid sinus and the carotid sinus syndrome per se is good. To avoid errors, one should realize that a hyperactive carotid sinus reflex may be only incidental and of no clinical significance[8]. Many patients with mild symptoms are not affected seriously but those with serious symptoms may be greatly handicapped. It is possible that in rare instances marked spontaneous carotid sinus overactivity may be the cause of cerebral vascular accidents. Hemiplegia in one of my patients could have been on this basis, although I could not prove it[6]. In any event, one can readily realize the danger in certain occupations and in patients driving cars.

In general, prognosis depends upon associated diseases. As previously mentioned in the sections on etiology and diagnosis the carotid sinus syndrome is often associated with advanced arteriosclerosis, especially coronary and cerebral, and hypertension, so accurate prognosis requires the evaluation of these diseases.

Summary

The hyperactive carotid sinus reflex and the carotid sinus syndrome are discussed.

The carotid sinus syndrome is an important disease that is commonly overlooked and is doubtless more frequent than generally realized.

It should be suspected in all patients with dizziness, faintness, syncope, and convulsions.

Diagnosis depends upon the history and reproduction of identical attacks by carotid sinus pressure.

It is primarily a disease of males in the upper age brackets.

Prognosis and importance in insurance medicine depend mainly upon the seriousness of associated diseases predominantly coronary and cerebral vascular disease and hypertension. These should be looked for and evaluated in all patients with symptoms of carotid sinus overactivity.

(editorial note: references identified upon request)

Indications for Surgery of Chronic Peptic Ulcers

BORRIS A. KORNBLITH, A.B., M.D., F.A.C.S.

Fellow New York Academy of Medicine, Attending Surgeon Gouverneur Hospital, New York, N.Y. — Diplomate American Board of Surgery

The accepted indications for surgery of chronic peptic ulcers are: 1) acute perforation, 2) persistent gastric retention due to pyloric obstruction, 3) persistent unrelieved abdominal pain and 4) hemorrhage from the ulcer bed either massive or recurrent.

A constructively critical evaluation of these indications is essential in reaching a decision as to whether or not to operate and which operation to utilize in the individual case at hand.

In general, peptic ulcer may be handled medically and will respond to conservative management in about 65% to 85% of the cases so treated. We shall concern ourselves with the failures of this type of management. Adequate medical care must include a bland diet, adequate alkalies, increased rest and avoidance of undue emotional stress. There should be constant supervision of the patient by his general practitioner who must spend a great deal of time in getting the patient's cooperation. Such cooperation may insure success of therapy while its lack may eventuate in the progression of the ulcer, necessitating surgery.

The surgery of peptic ulcer is essentially surgery of the complications produced by unfavorable progression of the ulceration. i.e.: acute perforation due to extension of the ulcer into the free pertoneal cavity: 2) gastric retention due to scarring and eventual narrowing of the pyloric ring followed by obstruction: 3) persistent pain due to penetration of the ulcer into adjacent structures such as the pancreas, the liver, the common hepatic duct, the colon or the gall bladder: and 4) hemorrhage due to erosion of a blood vessel, usually the pancreaticoduodenal or left gastric artery.

Acute Perforation of Peptic Ulcers

The salient features that indicate perforation are a history of upper abdominal discomfort, belching, vomiting and possibly a knowledge that a peptic ulcer was present.[1] About 85% of patients with perforation give a history of previous ulcer. A smaller number (7%) give a history of previous operation and about 5% give a history of a previous perforation.[2]

The physical findings vary with the peritoneal area involved, ranging from very meager abdominal tenderness in the right upper quad-

rant to that of board-like rigidity of the entire abdomen. The presence of air under the diaphragm may be demonstrable in about 70% of the cases and may be associated with absence of liver dullness. However, these signs should be relied upon only as confirmatories and their absence should not deter the surgeon from early operation.

The operation of choice is an exploratory laparotomy through a right upper rectus incision. The ulcer is located and closed over. The abdominal cavity is closed without draining as a rule. The exception is the case having extensive contamination of the general peritoneal cavity. In such cases supra-pubic drainage with a drain in the pelvis and possible drainage in the flank regions may be of value.

The overall operative motality of suture of perforation is about 12% to 15%. The mortality is dependent upon:

1) Early operation: Within the first four hours after perforation the mortality is low. After that period the mortality rate rises rapidly.

2) Extent of perforation and spontaneous sealing of the perforation: If the perforation has sealed off spontaneously numerous cases heal without operation. It is not uncommon to find a patient with a history and findings of perforation whose condition is critical and not suitable for surgery get well under conservative management. The stomach is emptied by means of a Levine tube and the fluid and electrolyte balance maintained by giving 3,000 c.c. of fluid a day intravenously, of which 1,000 c.c. is normal saline and the remainder made up with Amigen, 500 to 1,000 c.c. and 5% glucose in sterile water and transfusions of whole blood as needed. If the perforation spills gastroduodenal material into the free peritoneal cavity the time element of operating is of the greatest importance. Earliest possible operation is thus advised.

Despite some reports of conservative management of perforated peptic ulcers it is the consensus of opinion that surgery is imperative.

The closing of the perforation is the most important step to save life. However, there have been suggestions that closure might be accompanied by a simultaneous gastrojejunostomy. This is not advisable since the rationale of gastroenterostomy itself has not withstood the test of time because of subsequent gastrojejunal ulceration.

An immediate subtotal gastrectomy has also been used. This type of procedure is risky even in the best hands and should be reserved for a later date and is not advised since it would undoubtedly raise the operative mortality rate.

What is the outlook of suture of perforation alone? In general cases of peptic ulcer who were operated for perforations have a 30% rate of recurrence of symptoms for which further definitive surgery becomes necessary at a later date.

Persistent Gastric Retention Due to Pyloric Obstruction

Subtotal gastric resection if possible or gastroenterostomy as an alternative procedure with or without infradiaphragmatic vagotomy are the surgical procedures indicated for this group of patients.[3]

These cases represent chronic callous ulcers which produce stenosis and obstruction as a result of healing for the most part. They are actually problems of upper intestinal obstruction with their associated complications of loss of weight, derangement of the electrolyte balance. i.e.: high urea low carbon dioxide combining power of the blood, low blood chlorides, dehydration and evidence of liver damage. In the relief of this condition preoperative preparation is as important as the surgical relief

of gastric retention. Approximately 20% of these cases are not suitable subjects for the extensive radical resection. This group consists of patients usually over 60 years of age with long standing ulcer disease and obstruction, in poor general condition with cardiorenal or vascular disease, diabetes, chronic pulmonary disease or cases of obesity.

The object of gastric resection is to reduce the gastric acidity and removal of the lesion if possible. Since gastroenterostomy alone does not accomplish this the addition of vagotomy may prove of real value by removing the neurozenic phase of gastric secretion. Since the most important consideration among this group is the relief of obstruction gastroenterostomy can be used with good results.

The mortality rate of resection in this group varies between 7% and 10%.

Persistent Unrelieved Abdominal Pain

Among this group of patients are those with penetrating lesions which involve the peritoneal structures such extend to adjacent structures such as the pancreas, the liver, the common hepatic duct, the gall bladder or the colon.

The operation of choice among this group is again subtotal gastrectomy. Removal of the ulcer is performed only when such removal will not produce more damage than good. The ulcer may be excluded and left in situ or the duodenal closure may be accomplished by dissecting the duodenal stump away from the ulcer bed distal to the ulcer and then invert, and leave the ulcer bed where it is. Where the common hepatic duct is involved "T" tube drainage may be necessary. Any other complication must be handled individually as it arises.

The morbidity and mortality among this group is higher than gastrectomy alone in proportion to the extent of the complications present.

Bleeding Peptic Ulcers

In the final analysis, the treatment of bleeding peptic ulcers consists of subtotal gastric resection with resection of the ulcer where possible or subtotal resection with exclusion of the ulcer if resection is hazardous. The points at issue are, when to operate and under what conditions to postpone operation. It can be presumed that hemorrhage commits the surgeon to operation, sooner or later.

Finsterer[4] reviews the history of bleeding peptic ulcer and the conflicting statistics from many sources advocating "immediate" operation versus conservative therapy. The mortality rates given in the literature range between 5% to 12% for non-operative management as compared with 7% to 50% mortality for cases operated upon early. The statistics are obviously of no assistance in the individual case. The discrepancies are the result of making fixed deductions from incomparable cases.

Cole[5] states that, "the decision as to whether surgical or conservative treatment should be followed in the care of massive hemmorrhage from a peptic ulcer is one of the most difficult encountered by the medical profession."

The factors that are so difficult to evaluate are: 1. will the patient go on to exsanguination and death? or 2. will the bleeding stop? 3. is there a definite diagnosis as to the source of bleeding? 4. will transfusion and oxygen therapy be of value? 5. how long can one wait to reach a decision without jeopardizing the life of the patient?

To begin with, the immediate treatment of bleeding peptic ulcer consists of combating varying degrees of shock due to hemorrhage. Shock may be defined as a physiologic maladjustment in the transportation of oxygen by way of the blood stream to vital organs. The essential treatment of shock due to hem-

orrhage is whole blood replacement by transfusion and administration of oxygen in addition to other supportive measures. Acute shock can be combatted relatively easily if enough blood is available for transfusion. Chronic shock presupposes a more or less irreversible state of physiologic derangement in the vital organs, i.e.: the liver, kidneys, heart and brain as a result of oxygen deprivation over a prolonged period during the course of prolonged or recurrent hemorrhage. When such a state is reached the patient becomes a poor surgical risk or presents a definite contraindication to any surgical intervention until the vital organs are restored to relatively normal activity. This takes time; weeks to months.

Essentially, the foregoing considerations pertaining to avoidance of chronic irreversible shock form the basis for advocating immediate or early operation. However, the mortality rate is undoubtedly higher among interval cases. Operating conditions must be close to ideal in the early cases for success. In many centers there are emergency teams which consist of an internist, a surgeon, a resident staff and transfusion team ready to operate on quick notice. Preoperative preparation is at best inferior to the interval case and the postoperative course is not as smooth. Thus, there are sufficient reasons to postpone operation, especially since recovery from an initial hemorrhage is rather the rule than the exception.

It is of course of the greatest importance to observe such a patient carefully for any change of condition in the first 48 hours after hemorrhage has taken place. If there is evidence of a second episode of acute bleeding it is well to transfuse the patient, raise his blood pressure, increase his blood volume and operate promptly. If improvement has taken place it may perhaps be more advantageous to wait and operate between 6 weeks and 2 months after recovery.

It should be noted that about 20% of people with massive hemorrhage from a peptic ulcer do not have an antecedent ulcer history. If the patient can tolerate the procedure at all, diagnosis should be established by x-rays of the stomach with barium.

Mild hemorrhage which does not result in shock or a preshock condition with tarry stools as the only symptom is not uncommon and is not an urgent indication for operation.

Massive hemorrhage with ensuing shock should be treated without delay. It is generally accepted now that transfusion is of the greatest value. Whole blood and not plasma should be used because of the need of the oxygen carrying capacity of the red blood cells. As late as 1935 there were still those who went as far as to contraindicate any transfusion during acute hemorrhage. The reason given was that an increase in blood pressure might dislodge a thrombus which was formed at the site of bleeding while the blood pressure was low. The present methods of citrate transfusions given slowly, 15 to 20 drops per minute, obliviate sudden increases in blood volume and deleterious changes in hemodynamics.[6] There were times even 25 years ago when a transfusion was an operating room procedure and giving 1,000 c.c. of blood was thought to be a great deal. Under present conditions 5 to 6 liters may be necessary in a single case given slowly to maintain life and prepare a patient for operation after acute massive hemorrhage. Thus the indications for surgery in this group of patients still presents a difficult problem which must be individualized to a great extent.

Vagotomy Versus Gastric Resection

By now, there has been sufficient indication that vagotomy alone can

not be relied upon as a cure for peptic ulcer. Vagotomy with gastroenteroctomy has been advocated recently and the final results are apparently no better than those of gastrectomy alone. Healy's most recent report does not favor vagotomy. This subject must wait for further clarification.[7]

Gastric Ulcers

The problem of peptic ulcer of the stomach must be viewed in a different light from that of peptic ulcer of the duodenum.[8] Generally speaking gastric ulcer is a surgical condition. The association of gastric cancer with a preexisting ulcer; the development of malignancy in a gastric ulcer or the presence of a sloughed out carcinoma of the stomach which becomes an apparent ulcer, present sufficient indications for urgent early operation and gastric resection.

In a recent series about 12% of cases diagnosed as benign gastric ulcer proved to be malignant upon surgical exploration.[9]

All the criteria used to differentiate a benign from a malignant gastric lesion have large margins of error in the borderline case.

What are these criteria?

1. The site of the lesion: This is misleading. In one series two thirds of prepyloric lesions and over 50% greater lesions were found to be benign. The general belief is that these locations show a predilection for malignancy.

2. The size of the lesion: This too is of little assistance. At least one tenth of gastric ulcers are over four cms. in diameter or over and are benign.

3. Absence of free acid: The author has seen a case of 140 free acid and 180 total acid in a case that proved to be carcinoma. The presence of free acid is not uncommon in malignancy.

Age of the Patient

Benign ulcers are not uncommon in older people.

Recession after Treatment

It is very common to observe recession of the inflammatory reaction about an ulcer or carcinoma after adequate rest and palliative treatment.

Eosphagoscopy

In borderline cases inspection of the lesion even after resection by a competent pathologist is inconclusive.

Biopsy Through the Esophagoscope

Again, this is unsatisfactory. The lesion may be demonstrable histalogically only in the deeper layers of the ulcer and not approachable from the outside.

Histologic Examination after Resection

This means comes closest to determining the exact nature of the lesion in a borderline case. Even here numerous sections from different parts of the lesion are necessary.

Discussion

What surgical procedures should be advised for the patient with chronic peptic ulcer? The procedures generally agreed upon are:

1. Closure of the perforation in cases of perforated gastric or duodenal ulcer.

2. Subtotal gastrectomy if possible or alternative gastroenterostomy if the patient's condition does not warrant the more radical procedure in cases of pyloric obstruction.

3. Subtotal gastrectomy for all gastric ulcers.

4. Subtotal gastrectomy with or without exclusion of the duodenal ulcer for chronic penetrating duodenal ulcers.

5. Vagotomy: This operation reserved at present for the treatment of gastrojejunal ulcer and cannot be relied upon alone or with gastroenterostomy for the definitive treatment of chronic peptic ulcer.

(Editorial note: references identified upon request)

CASE PRESENTATION

Thromboangiitis Obliterans

The case of a 32 year old male patient was presented. His previous medical history was non-contributory with exception of several episodes of recurring phlebitis of the lower extremities within the last two years. His main complaints were coldness in legs and feet, sometimes associated with pain, particularly when walking, so that — within the past week—he had been unable to walk more than two blocks from his home. Furthermore, he complained of fatigue, frequent headaches and episodes of diplopia.

The examination showed a rather well nourished, a little obese young man, who appeared to be emotionally upset. He stated that he was worrying about his job as a gas station service man which kept him on his feet all day. He was married and had two small children. He had been smoking cigarettes heavily since adolescence. Heart, lungs, and abdomen did not reveal any pathology; chest x-ray picture and G.I. series were within normal limits. All laboratory tests were negative with exception of the fact that on various occasions the urinalysis showed 1 plus sugar. The fasting blood sugar was 130 mg. per cent and the blood sugar tolerance test showed a curve of 130, 190, 175, 150. Thus, the diagnosis of a mild diabetes mellitus was made. The feet appeared cold and the pedal pulses could not be felt. There were trophic changes of the nails of the toes present. When the legs were kept in a hanging position the distal parts displayed cyanosis. The circulatory function tests corroborated impaired circulation of feet and legs. The blood pressure was 138/89. The examination of the eye fundus did not reveal any gross abmormalities, although the patient maintained his complaints of occasional diplopia and reading difficulties. While the opinion of the staff members as to the diagnosis of this syndrome was unanimous: thromboangiitis obliterans (Buerger's disease), the views as to the proper treatment in this case were divided. Some staff members recommended a trial with tetraethylammonium chloride, which has shown promising results particularly in younger patients. The intravenous injection of ether was also mentioned by one resident physician; yet, most doctors felt that the reports in the literature would not encourage this procedure. The majority were in favor of sympathectomy; yet, some physicians objected as sympathectomy would only take care of the symptoms and signs of the lower extremities and would not take into account the cerebral symptoms. One of these physicians referred to the French school, particularly Leriche, who combined ganglionectomy (with or without splanchnicetomy) with adrenalectomy.

It was decided, finally, to start the treatment with tetraethylammonium chloride and to observe the course of the disease before resorting to surgical intervention. Furthermore, a diabetic management with insulin and diet was to be instituted, and the patient was strictly prohibited from smoking. (Literature: S. W. Kramer. Pennsylvania Med. J. 49: 619, March 1945—M. Protas and A. G. Saidman, Med. Ann. Dist. of Columbia, 17:34, January 1949—R. Buxton. Surgery, 110:69, March 1948—J. B. Kinmoth, Lancet 2:7;7, Nov. 6, 1948—R. Leriche, Presse Med. 57: 539, June 15, 1949—H. M. Sadek and W. De Paula. Revista do Hosp. das Clinicas, 4:17, Jan. 1949—N. Anton Acta med. Scandinav. 108:502, 1941.

Benign Pericarditis

Acute benign pericarditis continues to be mistaken for especially acute myocardial infarction. Pain, precordial or substernal, occurring in a person of the precoronary age group, should suggest benign pericarditis. This is particularly true if there is a history of an antecedent respiratory infection, abnormal temperature, sweating, weakness and anxiety accompanying onset of pain. The significant diagnostic hint is exacerbation of pain on deep breathing. It is present at the outset, and this symptom means acute pericarditis or acute pleuropericarditis, not acute myocardial infarction. Abdominal pain radiation may be erroneoulsly diagnosed, for the thoracic origin of the pain may be entirely overlooked. Shallow and rapid respirations are an early and prominent symptom. The patient is generally unable to breathe in recumbent position. A diagnostic sign is the characteristic posture: sitting or forward or lateral leaning to relieve the pain. A pericardial friction rub is the final clinical sign; it is heard early in the disease and may be audible for a short time only. It is well localized, either in the pulmonic area or immediately to the left of the lower part of the sternum. X-ray examination frequently shows an increase of the heart shadow. Pericardial effusion may be the cause in some cases. A shocklike syndrome, manifested anxiety, ashy cyanosis, sweating, weakness, lowered blood pressure, bradycardia, nausea and vomiting was present at the onset in some degree in all patients. It was promptly relieved by parenteral administration of ¼ grain of morphine sulfate and 1/100 grain of atropine sulfate. An elevation of temperature, increase in leukocyte count and acceleration of the sedimentation rate occur with, or shortly after, the onset of pain. Serial EKGs are of utmost importance: the diagnosis of acute benign pericarditis can be made from the limb lead tracings: initial elevation of the S-T segment in one or more leads, with upright T waves; in later stages the segment may show an upward convexity, with deeply inverted "Coved' T waves as in acute myocardial infarction. The S-T Segment may remain elevated for weeks but generally returns to the isoelectric line in 3 to 7 days. Treatment with aureomycin and terramycin effected rapid symptomatic improvement unless one follows the clinical picture closely, in conjunction with repeated EKGs, acute benign pericarditis will continue to be mistaken for myocardial infarction. (O. F. Rosenow and C. J. Gross. Arch. Int. Med., 6:795, June 1951)

Lower Nephron Nephrosis-Complications

Resumption of diuresis after anuria in lower nephron nephrosis, although generally indicating a favorable prognosis, may still initiate a precarious condition especially during the days when the urine output is greater than normal. The following factors may be of importance: persistence of uremia, with nausea, vomiting and electrolyte imbalance even when anuria is not present any longer; effects of massive diuresis, with development of multiple electrolyte and fluid depletion states; effects of overtreatment as an already overburdened circulatory system may be further embarrassed by to much fluid and electrolyte therapy; intercurrent disease such as pulmonary or genitourinary system infections. (I. S. Ravin; P. R. Aronson and J. H. Yules. New England J. Med, 244:830, May 31, 1951)

THERAPEUTIC SUGGESTIONS

Pulmonary Tuberculosis

The authors stress that it is generally agreed that the best regimen available for most manifestations of the disease is the administration of streptomycin or dihydrostreptomycin two or three days each week, plus the daily administration of para-aminosalicylic acid. While the advantage of this treatment is that it carries little toxicity and that few strepomycin-resistant strains of tubercle bacilli are encountered, its disadvantage is that many patients cannot tolerate the large daily dose of para-aminosalicylic acid. The authors changed the treatment method in administering 1 mg. of dihydrostreptomycin intramuscularly on three alternate days of each week. On the same days the maximal tolerated dose of para-aminosalicylic acid was given orally in 3 or 4 doses, either as the free acid or the sodium salt. Most patients tolerated the drug when the sodium salt was used. The available daily intake of para-aminosalicylic acid in this form was 15 to 20 Gm. . . . "the clinical impression is that this regimen is as effective therapeutically as the daily administration of streptomycin and para-aminosalicylic acid." (A. G. Karlson; D. T. Carr; G. N. Hofmann and K. H. Pfuetze. Proc. Staff Meet., Mayo Clinic, 23:437, November 7, 1951).

Otomycosis

The author recommends as most valuable local application: 2% thymol in metacresylacetate (cresatin) applied full strength on a cotton wick. The cotton is left in the external canal for 24 hours. Then, the application is repeated if necessary. The results were satisfactory. (B. W. Chycock. J. of the Oklahoma State Med. Ass., 7:265, July 1951).

Aureomycin

A significant number of patients who received of aureomycin hydrochloride, orally, acquired moniliasis. The effect was observed from several lots of the drug. Preexisting cutaneous and mucous membrane lesions are probably predisposing factors. Aureomycin hydrochloride in 250 mg. capsules for oral administration stimulated the growth of Candida albicans, Cryptococcus neoformans, and Saccharomyces cerevisiae in vitro. The possibility that the growth factor is active in vivo might be an explanation for the increased incidence of moniliasis among patients treated with the drug. (R. B. Pappenfort, Jr., and E. Spitzer Schnall. Arch. Int. Med., 6:729, December 1951)

Herpes Gestationis

Milton suggested the term herpes gestationis for the characteristic cutaneous lesions, appearing in the form of grouped herpetic elements. Allen called the dermatosis 'dermatosis multiforme of pregnancy' and Brocq termed it 'dermatitis polymorpha' of gestation. It was observed that the skin lesions appeared in the first phases of pregnancy coinciding with the time in which the secretory activity of the chorioplacental system is considerably reduced to the production of chorionic gonadotropin. As the demonstration of excess chorionic gonadotropin during the final stages of pregnancy is related with an insufficient production of or an error in, progesterone metabolism, substitution therapy with this hormone was tried out. Doses of 50 mg. to 100 mg. proved to be sufficient to improve the skin condition markedly. A maintenance dose of half the initial was necessary to sustain the improvement. (C. Keaty P. E. Jones and J. H. Lamb. Arch. Dermatol. & Syphil. June 1951).

Allergic Headache

An impressive percentage of cases of frontal headache are relieved by ergomine drugs (Cafergot, consisting of 100 mg. caffeine and 1 mg. of ergotamine tartrate — 2 tablets at onset of symptoms, one tablet repeated every half hour up to 6 tablets; no more than ten tablets pro weak). Frontal headache may be associated with respiratory allergy; therefore, if present, it should be correctly managed. Food sensitization may be a factor in many cases. There should be a cooperation of allergist and psychiatrist. (H. D. Ogden. Annals Allergy, 5:611 September-October 1951)

Cirrhosis of the Liver

It is difficult to discover cirrhosis of the liver in office practice the complaints are usually nonspecific: fatigue, loss of energy, anorexia, anxiety, sleeplessness, occasionally discomfort in the right upper abdominal quadrant. In the previous history one generally finds overindulgence in alcohol; rarely jaundice, fever and chills. The liver is usually palpable 2 to 3 cm. below the right costal margin. The other more pronounced signs such as ascites, increased collateral circulation of the abdomen, spider angiomas, hepatic facies, etc. are almost never seen. The bromsulfalein retention test is in most cases the only test giving a positive result. Liver biopsy reveals moderately fatty infiltration with slight hepatic cellular necrosis, considerable chronic inflammation, and early invasive fibrosis. Therapy should be started, even if biopsy is not available: moderated increase in protein intake, vitamin supplements and interdiction of alcohol. Untreated patients in these early stages may show a progressive lesion with terminal advanced Laennec's cirrhosis. (W. D. Davis, Jr., New Orleans Med. & Surg. J. 5:192, November 1951).

Obesity

Author reports on 64 patients who did not lose weight on a dietary treatment during a six month period. They were treated with Dexamyl (a combination of Dexedrine and amytal) for control of appetite. 59 of these patients, within three months, lost considerable weight; 14 reached their normal weight and 28 reduced to within 19% of normal weight. The drug was safely and successfully administered to 10 diabetic and 7 hypertensive patients. (E. Roberts. Ann. Int. Med. 6:1324, June 1951).

Thyroid Crisis

Report on 25 crises seen in 484 patients with hyperthyroidism. The patient's increased muscular activity increases his heat production which already is elevated due to thyrotoxicosis; the oxygen demand causes rapid breathing with again increased heat production. Profound sedation, oxygen tent, cooling with ice packs are the therapeutic measures recommended. (J. D. Rives and R. N. Shepard. Am. Surgeon, 17:406, May 1951).

Chalazion

Chalazion is a chronic often secondarily inflammatory swelling of the Meibomian gland of the eyelid. After the infection has set in, the treatment is exclusively surgical. Author has, for several years, used 50,000 to 100,000 U of vitamin A in the treatment of the early chalazion and also as a preventive measure following surgical removal on the chronically infected Meibomian glands. The results have been favorable; early chalazion disappeared and as the treatment was continued for several weeks, no complications were observed. Even a severe case of multiple chalazion of both lids was cured by high doses of Vitamin A. (C. S. Hickey. The Eye, Ear, Nose and Throat Monthly, 9:488 Sept. 1951).

Books on Internal Medicine

A timely book on blood banking[1] which is not only useful for hospital offices but also for the general practitioner furnishes ample yet well selected and well styled explanation on grouping, typing and banking of blood. We consider it as one of the most valuable presentations on this subject. Together with this work an excellent, concise and clear treatise on hematology should be recommended.[2] The illustrations are good and the explanatory text is nourished by experience and judiciousness. Adrenal Insufficiency is one of the most actual medical subjects.[3] Dr. Thorn's book outlines the physiology, the diagnostic tests, and the significance of the adrenal hormones, including the commercial preparations. The exposition of Addison's Disease is lucid. An exceedingly revealing book, both scientifically and practically, is Dr. Wiggers'[4] work on shock. For the general practitioner the second chapter dealing with the symptomatology of shock is particularly serviceable. Considering the importance of this subject, the book should be read widely. The writing on the problem of arthritis seems to be inexhaustible. Dr. Lewin's book is directed to the layman.[5] As there is so much inexpert publicity about arthritis and rheumatism in the lay-press, a discerning and well balanced information such as this should be welcomed. Dr. Morris Fishbein has prepared the foreword. Dr. Selye has carried on his publication on stress[6] in his annual report of 1951. Everybody interested in these problems will obtain a wealth of knowledge. The book is thought to be reference work on the yearly progress. A new book on peptic ulcer[7] is edited by Dr. Sandweiss. The value of the presentation becomes evident as 77 authorities on peptic ulcer are contributors to this volume. The book deals with all the aspects of the problems involved: anatomy and physiology, pathogenesis and etiology, diagnosis, medical and surgical treatment, complications. A very comprehensive and thorough book on dietetics[8] should be mentioned. It is not one of the man expatiations on this often treated topic; it is a scientifically relevant and practically pertinent source of information. An interesting publication on individual metabolic patterns[9] of syndromes, dealing with the whole metabolic picture as reflected by characteristic patterns of measurement, comes to a number of conclusions, which are essential.

1. *Grouping Typing and Banking of Blood.* By Otokar Jaroslav Pollak, M.D. Charles C. Thomas, Publisher. Springfield, Ill. 100 pages. Cloth. 1951.
2. *Color Atlas of Morphologic Hematology. With A Guide to Clinical Interpretation.* By Geneva A. Dalnd. 74 pages. Cloth. Harvard University Press, Cambridge, Mass. 1951. $5.
3. *The Diagnosis and Treatment of Adrenal Insufficiency.* By George W. Thorn, M.D. Charles C. Thomas, Publisher. Springfield, Ill. 1951. 180 pages. Cloth. $5.5.
4. *The Physiology of Shock.* By Carl J. Wiggers, M.D. The Commonwealth Fund, New York. Published by Harvard University Press, 1950. 459 pages. Cloth $5.
5. *Arthritis and Rheumatic Diseases.* By Philip Lewin, M.D. McGraw-Hill Book Company, New York, 1951. 175 pages. Cloth. $3.50.
6. *Annual Report on Stress.* By Hans Selye, M.D. Acta Inc., Medical Uublishers. Montreal, Canada, 1951. 511 pages; 133 reference pages. Cloth. $10.
7. Peptic Ulcer. Clinical Aspects. Management. D. J. Sandweiss. Editor. W. B. Saunders Company, Philadelphia. 1951. 700 pages. Cloth. $15.
8. *Modern Dietetics.* By Doris Johnson, M.S. Edited by Hazel E. Munsel, Ph. D. G. P. Putnam's Sons, New York, 1951, 5[illegible] pages. Cloth.
9. Biochemical Institute Studies, IV. Individual Metabolic Patterns and Human Disease: An Explanatory Study Utilizing Predominantly paper Chromatographic Methods, From the Biochemical Institute and the Department of Chemistry. The University of Texas and the Clayton Foundation for Research. Austin. The University of Texas. 205 pages. Paper.

NEW PHARMACEUTICAL PRODUCTS

Dorbane. 1,-8 dihydroxyanthraquinone is the active principle.
Indication: laxative, acting upon the large bowel exclusively. Dorbane Tablets containing 0.150 Gm dihydroxyanthraquinone for adults and Dorbane "Confects", 0.075 Gm. flavored wafers for children.
Schenley Laboratories, Inc., Lawrenceburg, Indiana

Dihydrocillin, Fortified. Each vial contains Crystalline Procaine Penicillin G, 300,000 units; Crystaline Sodium Penicillin G (Buffered), 100,000 units and Dihydrostreptomycin (sulfate), 1Gm. This combination is intended for preparing an aqueous suspension solution for intramuscular injection.
Indications: urinary tract infections, subacute bacterial endocarditis, peritonitis (mixed infections), acute gonococcal infections.
The Upjohn Company, Kalamazoo, Michigan

Bisulfa 250 M. Tablets. Containing: Crystalline Penicillin G Potassium, 250,000 units; Sulfadiazine, 0.167 Gm.; Sulfamerazine, 0.167 Gm.; Sulfamethazine, 0.167 Gm.
Indications: pneumonias, Vincent's angina, gonorrhea, follicular tonsillitis, mastoiditis, etc.
The Upjohn Company, Kalamazoo, Michigan.

Pregnancy

diagnosed in 20 minutes with

Carson-Saeks

C. P. T.
CHEMICAL PREGNANCY TEST
Patented

PROVEN ACCURATE[1,2,3], thru more than 4 years of clinical use.

FEATURES
*Simple office procedure
*No delay—accurate in early pregnancy
*Economical—costs less per test

AVAILABLE
Your physicians' supply dealer.

Ref. 1. Ricketts, W.A.; Carson, R.M. and Saeks, R.R.; Am. J. Obst. and Gynec. 56:955 (1948).
2. Cheval and Hans; Bruxelles Med. 32: 1677 (1950).
3. Paglari, H., Arch. Sci. Med., 89:89-98 (1950).

C. P. T. Laboratories
Dayton, Ohio

MODERN TREATMENT *Relieves* EYE IRRITATION

OPTREX is a refreshing, decongestive ocular lotion which quickly relieves ocular irritations, such as eye strain, resulting from close work, reading, movies, television, dust and wind, bright artificial lighting, fatigue.

OPTREX IS UNSURPASSED IN DAILY OCULAR HYGIENE and is prescribed and used by specialists throughout the world following treatment of the eyes.

The scientifically designed eye cup which comes with every bottle permits a soothing, antiseptic treatment of the entire surface of the eye and eyelids.

Your patients' eyes are important, see that they get the best of care. Prove for yourself how **OPTREX** will relieve eye strain. *Send for generous trial bottle.*

The Chemdrug Corp.
730 Fifth Avenue, New York 19, N.Y.

SEND FOR THIS LITERATURE

1. **Allergies** (colds)—new antihistamine
2. **Dietary deficiencies**—daily vitamin supply
6. **Respiratory stimulant**—for the newborn
3. **Respiratory infections**—penicillin inhalation
4. **Psoriasis**—oral drug
5. **Bronchial asthma**—sustained management
7. **Cough**—antitussive syrup and tablets
8. **Sulfonamide** — triple sulfa combination
9. **Rheumatic fever**—management
10. **Antihistamines**
11. **Functional Uterine Bleeding** — management
12. **Pain control**—saddle block and higher spinal analgesia
13. **Whooping cough**—relief
14. **Premature labor** — habitual and threatened abortion—management
15. **Congestive heart failure**—mercurial diuretic
16. **Birth control**—diaphragm and jelly
17. **Sore throat**—alkaline germicidal solution
18. **Cough**—management
19. **Acute bronchitis**—treatment
20. **Inflammatory glandular swelling**—topical decongestive treatment
21. **Insomnia**—gentle sedation
22. **Appetite**—tonic
23. **Functional amenorrhea** — management
24. **Peptic ulcer**—demulcent
25. **Postoperative abdominal distention** and urinary retention — prevention and management
26. **Hemorrhoids**—relief of pain and inflammation
27. **Skin affections**—therapy
28. **Gastric neurosis,** pyloris spasm, nausea—management
29. **Sedative**—without habit formation
30. **Arthralgia** (bursitis), lumbago—ointment
31. **Pregnancy test**
32. **Allergies**—management
33. **Bronchial asthma**—prolonged relief
34. **Infant feeding**—milk-free formula in allergic reactions
35. **Infant nutrition**—information
36. **Cough**—palatable creosote preparation
37. **Eye hygiene**—decongestive lotion
38. **Headache,** neuralgia—pain relief
39. **Obesity**—dietary management
40. **Arthritis**—colloidal gold sulfide therapy
41. **Trichomoniasis,** moniliasis—vaginal suppositories
42. **Asthma**—symptomatic relief
43. **Pruritus**—management
44. **Cardiovascular disorders** — management
45. **Blood sugar**—12 minute test
46. **Urinalysis**—1 minute test
47. **Gout, Gouty Arthritis**—specific therapy
48. **Allergies** (food, inhalant, contact, etc.)—new parenteral therapy
49. **Dermatologic Conditions**—new parenteral therapy
50. **Ophthalmologic Conditions**—new parenteral therapy
51. **Acne and Pruritis Ani**—a cutaneous vasoconstrictor
52. **Arthritis**—a skeletal muscle relaxant
53. **Gastrointestinal and genitourinary spacticity**—a smooth muscle relaxant and sedative.
54. **Peripheral vascular disorder**—a vasodialator

Use Postage Free Card for Ordering Free Literature

UNIV
OF M
PR
ME
LIB
General Library
Ann Arbor